

## Complete Summary

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### GUIDELINE TITLE

Practice parameters for the treatment of restless legs syndrome and periodic limb movement disorder.

### BIBLIOGRAPHIC SOURCE(S)

American Academy of Sleep Medicine. Practice parameters for the treatment of restless legs syndrome and periodic limb movement disorder. Sleep 1999 Nov 1;22(7):961-8. [33 references]

## COMPLETE SUMMARY CONTENT

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## SCOPE

### DISEASE/CONDITION(S)

Restless legs syndrome and periodic limb movement disorder

### GUIDELINE CATEGORY

Treatment

### CLINICAL SPECIALTY

Neurology  
 Sleep Medicine

### INTENDED USERS

Physicians

### GUIDELINE OBJECTIVE(S)

To provide recommendations for the practice of sleep medicine in North America regarding the treatment of restless leg syndrome and/or periodic limb movement disorder.

## TARGET POPULATION

Patients in North America with restless legs syndrome and/or periodic limb movement disorder

## INTERVENTIONS AND PRACTICES CONSIDERED

1. Levodopa with decarboxylase inhibitor
2. Pergolid
3. Carbamazepine
4. Oxycodone
5. Propoxyphene
6. Clonazepam
7. Clonidine
8. Gabapentin

Note: Non-pharmacological therapies, such as accommodative strategies and sleep hygiene, behavioral and stimulation therapies, invasive therapies, and nutrition/diet, were considered.

## MAJOR OUTCOMES CONSIDERED

- Symptom relief
- Number of leg/limb movements, using measures from polysomnography [periodic limb movements in sleep; periodic limb movement index; periodic limb movement arousal index], actigraphy, and immobilization tests
- Quality of life, using measures of self-report on the Stanford Sleepiness Scale or the Epworth Sleepiness Scale and physiological assessment of sleepiness using the Multiple Sleep Latency Test

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)  
Hand-searches of Published Literature (Secondary Sources)  
Searches of Electronic Databases

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Medline (U.S. National Library of Medicine) searches for articles on restless leg syndrome and periodic limb movement disorder were conducted through April, 1998. Key words for search included restless legs, both as a subject or text word; a combination of myoclonus and periodic; a combination of sleep with dyskinesia, myoclonus, or restless; and a combination of sleep, periodic, and movements. This search led to 588 articles and was supplemented by review of Current Contents (Institute for Scientific Information [ISI]) and the Sleep Research indices

to September 1997 and by articles discovered during other research, if published prior to April 1998. 328 articles, identified as potentially relevant based on abstracts were obtained in full length and examined further. Articles to be entered into the evidence tables and used for the guideline developer's conclusions were required to be published after peer review and to meet two initial criteria: a minimum of 5 patients studied and a defined outcome that could be used to assess the therapy. Articles were eliminated in which there was inadequate definition of restless leg syndrome or periodic limb movement disorder or in which the numbers of patients involved could not be clearly determined. Articles in all languages were considered for inclusion. Forty-five articles relevant to therapy and meeting criteria were then selected for analysis and tabulation.

Some articles, more recent than the review paper timeline, but relevant to therapy of restless leg syndrome or periodic limb movement disorder are noted in the companion practice parameter paper.

131 articles derived from the search did not meet the criteria for reviewable therapeutic articles, but were found useful as background articles. These articles were in languages comprehensible to the task force members, which included English, French, German, Italian, and Spanish.

#### NUMBER OF SOURCE DOCUMENTS

328 articles were identified, 45 articles were selected for analysis and tabulation

#### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

#### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

##### Recommendation Grades

##### A (Evidence Level I)

- Randomized well-designed trials with low-alpha & low-beta errors\*

##### B (Evidence Level II)

- Randomized trials with high-beta errors\*

##### C (Evidence Level III)

- Nonrandomized controlled or concurrent cohort studies

##### C (Evidence Level IV)

- Nonrandomized historical cohort studies

## C (Evidence Level V)

- Case series

\* Alpha error refers to the probability (generally set at 95% or greater) that a significant result (e.g.,  $p < 0.05$ ) is the correct conclusion of the study or studies. Beta error refers to the probability (generally set at 80% or 90% or greater) that a nonsignificant result (e.g.,  $p > 0.05$ ) is the correct conclusion of the study or studies. The estimation of beta error is generally the result of a power analysis. The power analysis includes a sample size analysis which projects the size of the study population necessary to ensure that significant differences will be observed if actually present.

## METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Two task force members analyzed each of the articles for design, definition of restless leg syndrome and periodic limb movement disorder, exclusion and inclusion factors, subject character and dropout, outcome measures, side effects evaluated, biases, and conclusions. Discrepancies were resolved and 6 evidence tables were prepared based on the analyses.

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

## DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

When scientific data were insufficient or inconclusive, recommendations were based on consensus opinion.

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Levels of Recommendation

Standard

- This is a generally accepted patient-care strategy which reflects a high degree of clinical certainty. The term standard generally implies the use of Level I Evidence, which directly addresses the clinical issue, or overwhelming Level II Evidence.

Guideline

- This is a patient-care strategy which reflects a moderate degree of clinical certainty. The term guideline implies the use of Level II Evidence or a consensus of Level III Evidence.

#### Option

- This is a patient-care strategy which reflects uncertain clinical use. The term option implies either inconclusive or conflicting evidence or conflicting expert opinion.

### COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

### METHOD OF GUIDELINE VALIDATION

Internal Peer Review

### DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The Board of Directors of the American Academy of Sleep Medicine approved these recommendations.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

Recommendations are given as standards, guidelines, or options, and unless otherwise specified, are supported by Level II to Level V evidence according to the definitions given at the end of the Major Recommendations field.

#### A. General treatment and safety recommendations

1. Pharmacological treatment of restless leg syndrome and/or periodic limb movement disorder should be limited to patients who meet specific diagnostic criteria (Hening, et al., 1999, sections 3.1 and 5.1) (Standard).
2. The physician who evaluates and treats patients with restless leg syndrome and/or periodic limb movement disorder should be aware of the existence of idiopathic and secondary forms, and should be knowledgeable about risk factors and co-morbid conditions for these disorders (Hening, et al., 1999, section 3.1.2.2) (Standard).
3. Individuals with restless leg syndrome and/or periodic limb movement disorder who are being treated with medication should be followed by a physician at appropriate intervals and monitored for adverse side effects, augmentation, and tolerance (Hening, et al., 1999, sections 4.0 and 5.0) (Standard).

#### B. Specific treatment recommendations

1. Levodopa with decarboxylase inhibitor and pergolide are effective in the treatment of restless leg syndrome and periodic limb movement disorder (Hening, et al., 1999, section 4.2.1) (Guideline).

2. Oxycodone and propoxyphene are effective in the treatment of restless leg syndrome and periodic limb movement disorder (Hening, et al., 1999, section 4.2.2) (Guideline).
3. Carbamazepine is effective in the treatment of restless leg syndrome (Hening, et al., 1999, sections 4.2.4 and 5.1) (Guideline).
4. Clonazepam is effective in the treatment of periodic limb movement disorder and possibly restless leg syndrome (Hening, et al., 1999, section 4.2.3) (Option).
5. Gabapentin is effective in the treatment of restless leg syndrome (Hening, et al., 1999, sections 4.2.4 and 5.1) (Option).
6. Clonidine is effective in the treatment of restless leg syndrome (Hening, et al., 1999, section 4.2.5) (Option).
7. Iron supplementation is effective in the treatment of restless leg syndrome in patients with iron deficiency (Hening, et al., 1999, sections 4.2.6.2 and 5.2) (Option).
8. No specific recommendations can be made regarding treatment of pregnant women with restless leg syndrome or periodic limb movement disorder (Hening, et al., 1999, section 5.4).
9. No specific recommendations can be made regarding treatment of children with restless leg syndrome or periodic limb movement disorder (Hening, et al., 1999, section 5.4).

#### Definitions:

#### Recommendation Grades

##### A (Evidence Level I)

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The power analysis includes a sample size analysis which projects the size of the study population necessary to ensure that significant differences will be observed if actually present.

#### Levels of Recommendation

##### Standard

- This is a generally accepted patient-care strategy which reflects a high degree of clinical certainty. The term standard generally implies the use of Level I Evidence, which directly addresses the clinical issue, or overwhelming Level II Evidence.

##### Guideline

- This is a patient-care strategy which reflects a moderate degree of clinical certainty. The term guideline implies the use of Level II Evidence or a consensus of Level III Evidence.

##### Option

- This is a patient-care strategy which reflects uncertain clinical use. The term option implies either inconclusive or conflicting evidence or conflicting expert opinion.

#### CLINICAL ALGORITHM(S)

A treatment flow diagram for symptomatic restless leg syndrome or periodic limb movement disorder patients is provided in the guideline document.

### EVIDENCE SUPPORTING THE RECOMMENDATIONS

#### REFERENCES SUPPORTING THE RECOMMENDATIONS

[References open in a new window](#)

#### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

In most cases the conclusions are based on evidence from studies published in peer-reviewed journals which were evaluated as noted in the evidence tables in the accompanying background paper. However, when scientific data are absent, insufficient or inconclusive, the recommendations are based upon consensus opinion. The strength of each recommendation is based on the level of the evidence available. The type of evidence supporting each recommendation is identified in the "Major Recommendations" field.

### BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

#### POTENTIAL BENEFITS

- Reduced symptoms associated with restless leg syndrome and/or periodic limb movement disorder
- Improved sleep quality
- Improved quality of life

## POTENTIAL HARMS

A number of significant complications of treatment have been noted, especially with use of dopaminergic agents. They include:

- Rebound effects: the tendency of symptoms to worsen at the end of a dosing period, leading to late night or morning recurrence of symptoms and periodic limb movements in sleep.
- Augmentation: the apparent worsening of symptoms seen with long-term use of the medications (seen most commonly with levodopa and is increased with higher doses). Symptoms of augmentation may present as progressively earlier daily onset of restless leg syndrome symptoms; consist of expansion of the symptoms beyond the legs (involving trunk and upper limbs) and may be seen as an increase in symptom intensity or decrease in drug efficacy.
- Transient aggravation of symptoms for several days at cessation of restless leg syndrome therapy

Refer to Table 1 of the original practice parameter for important and detailed information regarding the side effects of medications that have been used for the treatment of restless leg syndrome and periodic limb movement disorder. Note however that Table 1 in the original practice parameter is based on a sample of representative articles from the therapeutic literature. Some of the listed side effects are reported at treatment doses used in disorders other than restless leg syndrome/periodic limb movement disorder and may not be as likely to occur in dosage schedules as recommended for restless leg syndrome/periodic limb movement disorder. In addition, data on side effects may change as new evidence appears; therefore, updated Physician's Desk References should be consulted.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

- These practice parameters define principles of practice that should meet the needs of most patients in most clinical situations. These guidelines should not, however, be considered inclusive of all proper methods of care or exclusive of other methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding the propriety of any specific care must be made by the practitioner in light of the individual circumstances presented by the patient and the available diagnostic and treatment options and resources.
- For the use of medication, data regarding side effects, medication effects, and the need for monitoring patients (clinically and by laboratory parameters) are based on information available to the guideline developer at the time of guideline development. The reader should refer to the updated Physicians Desk Reference and literature for any new information which might influence these guidelines.

- Several articles have been published since closure of the review paper MEDLINE search which may be relevant to clinical decision making. Articles on dopamine agents including pramipexole, pergolide, and L-dopa, gabapentine, and magnesium therapy are available. The reader is urged to seek these and additional new articles appearing this active area of research.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Living with Illness

### IOM DOMAIN

Effectiveness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

American Academy of Sleep Medicine. Practice parameters for the treatment of restless legs syndrome and periodic limb movement disorder. Sleep 1999 Nov 1;22(7):961-8. [33 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

1999

### GUIDELINE DEVELOPER(S)

American Academy of Sleep Medicine - Professional Association

### SOURCE(S) OF FUNDING

American Academy of Sleep Medicine

### GUIDELINE COMMITTEE

## Standards of Practice Committee

### COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Names of Committee Members: Andrew L. Chesson, Jr; Merrill Wise; David Davila; Stephen Johnson; Michael Littner; W. McDowell Anderson; Kristyna Hartse; Jose Rafecas.

### FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All members of the American Academy of Sleep Medicine's Standards of Practice Committee and Board of Directors completed detailed conflict-of-interest statements and were found to have no conflicts of interest with regard to this subject.

### GUIDELINE STATUS

This is the current release of this guideline.

According to the guideline developer, this guideline is currently under revision. The revised guideline is expected to be available in March 2002. NGC will update this Summary when the updated guideline is available.

### GUIDELINE AVAILABILITY

Print copies: Available from the Standards of Practice Committee, American Academy of Sleep Medicine, One Westbrook Corporate Center, Suite 920, Westchester, IL 60154. Web site: [www.aasmnet.org](http://www.aasmnet.org).

### AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Hening W; Allen R; Earley C; Kushida C; Picchietti D; Silber M. The treatment of restless legs syndrome and periodic limb movement disorder. An American Academy of Sleep Medicine Review. Sleep 1999 Nov 1;22(7):970-99.

Print copies: Available from the Standards of Practice Committee, American Academy of Sleep Medicine, One Westbrook Corporate Center, Suite 920, Westchester, IL 60154. Web site: [www.aasmnet.org](http://www.aasmnet.org).

### PATIENT RESOURCES

None available

### NGC STATUS

This summary was completed by ECRI on December 19, 2000. The information was verified by the guideline developer on January 15, 2001.

## COPYRIGHT STATEMENT

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